

## **REMARKS**

The Applicants acknowledge the Examiner's comprehensive Office Action with appreciation. Claims 4-6 are pending in the application. The previous rejections under 35 USC § 112, first and second paragraphs have been withdrawn in view of the Response and Amendment filed on February 12, 2008; however, the Office raises a new rejection under 35 USC § 112, first paragraph. The Office also raises a prior art rejection under 35 USC § 103.

Claims 4-6 are rejected for lack of enablement under 35 USC § 112, first paragraph. It is the position of the Office that the specification, while being enabling for the treatment of gastro-duodenal pain does not reasonably provide enablement for the treatment of gastritis or duodenitis. The Office goes on to state that the terms gastritis and duodenitis are very broad since these terms encompass generic symptoms which are associated with disparate conditions involving inflammation of the stomach lining (in the case of gastritis) or inflammation of the duodenum (in the case of duodenitis). It is the position of the Office that one skilled in the art would recognize the treatment of such conditions to be "highly unpredictable." The Office goes on to state that the applicant has provided no evidence that the compound of the instantly claimed method is effective in the treatment of gastritis and/or duodenitis as such symptoms manifest in numerous undefined conditions.

With the instant Amendment, Claim 4 has been amended to limit the condition claimed to be treatable to gastro-duodenal pain, which condition is acknowledged as enabled by the Office. Moreover, dependent Claims 5 and 6 have been amended to limit the claimed conditions to "pain associated with gastritis" and "pain associated with duodenitis", respectively. Support for this amendment may be found at page 2 of the specification, and the Applicants respectfully submit that no new matter has been introduced by this amendment. Thus, the Applicants respectfully submit that the instant claims, as amended, comply with the enablement requirement under 35 USC § 112, first paragraph. Reconsideration and withdrawal of the enablement is respectfully requested.

Claims 4-6 are rejected for obviousness under 35 USC § 103(a) based on the disclosure of Lachiarriere, et al. (US Patent No. 5,866,168) in view of Wierzbicki, et al. (US Patent No. 5,128,367). The Office states that "for the purposes of applying art", the Office is interpreting gastritis and/or duodenitis as referring to the pain associated with these conditions and not the inflammation associated with the conditions.

It is the position of the Office that Lachiarriere, et al. disclose the use of strontium salts for the treatment of diseases which respond to substance P antagonism and that the reference also discloses that substance P is involved "in particular" in the transmission of pain. It is the further position of the Office that Lachiarriere, et al. disclose that substance P antagonists, including strontium salts, may be used to treat gastrointestinal diseases. The Office acknowledges that the Lachiarriere, et al. reference does not disclose the instant thiophene compound (i.e., the distrontium salt of 2-[N,N-di(carboxymethyl)amino]-3-cyano-4-carboxymethyl-thiophene-5-carboxylic acid).

It is the position of the Office that Wierzbicki, et al. disclose that the instant thiophene compound is pharmaceutically useful because it provides improved bioavailability. The Office acknowledges that the Wierzbicki, et al. reference does not disclose the use of the distrontium salt of 2-[N,N-di(carboxymethyl)amino]-3-cyano-4-carboxymethyl-thiophene-5-carboxylic acid for treating gastrointestinal diseases.

It is the position of the Office that, since Lachiarriere, et al. disclose that strontium salts are substance P antagonists and that such antagonists may be used to treat pain such as gastritis or duodenitis, one skilled in the art would have been motivated to employ the divalent strontium salt of 2-[N,N-di(carboxymethyl)amino]-3-cyano-4-carboxymethyl-thiophene-5-carboxylic acid disclosed in Wierzbicki, et al. for the treatment of pain, particularly in view of the "improved bioavailability" characteristics disclosed in Wierzbicki, et al.

The Applicants respectfully submit that Lachiarriere, et al. disclose that "[b]y virtue of the ubiquitous distribution of substance P, very many disorders are associated with an excessive synthesis and/or release of substance P." The reference goes on to disclose a lengthy list of conditions in which substance P is involved. The reference further discloses that lanthanide, manganese, tin, zinc, yttrium, cobalt, barium, and strontium salts exhibit substance P antagonizing activity and are therefore useful for the treatment and/or alleviation of pain associated with various skin disorders.

As noted above, the Office acknowledges that Lachiarriere, et al. do not disclose the instant thiophene compound. Moreover, the only specific examples of compositions comprising a strontium salt disclosed in Lachiarriere, et al. contain strontium chloride (Example 5) and glycerophosphate of strontium (Example 7). The Applicants respectfully submit that the Office has provided no teaching to demonstrate that one skilled in the art would have been motivated to replace the chloride ion or the glycerophosphate group of the Lachiarriere, et al. compositions with the structurally dissimilar thiophene compound disclosed in Wierzbicki, et al. The fact that these groups **could be** replaced with the thiophene compound disclosed in Wierzbicki, et al. is not sufficient to create a reasonable expectation of success to establish obviousness.

The courts have held that the mere fact that it might be **possible** to select elements of an invention by combining elements of references does not make out an obviousness rejection. See In re Bergel, 130 USPQ 206, 208 (CCPA) 1961). More recently, the Court of Appeals for the Federal Circuit has held that "mere identification in the prior art of each element is insufficient to defeat the patentability of the combined subject matter as a whole." In re Kahn, 78 USPQ2d 1329 (CAFC 2006)(cited with approval by the court in the KSR decision).

Moreover, with the instant Response, the Applicants provide a literature reference, Fisch, et al. (*Basic & Clinical Pharmacology & Toxicology*, **2006**, **98**, 442-446 – which reference is also listed on the attached Form PTO-1449), which speaks to the superior and unexpected effects associated with the distrontium salt of 2-[N,N-di(carboxymethyl)amino]-3-cyano-4-carboxymethyl-thiophene-5-carboxylic acid (i.e.,

the distrontium salt employed in the instantly claimed method) when compared to strontium chloride (i.e., the strontium salt contained in the composition of Example 5 disclosed in the Lachiariere, et al. reference). Specifically, the Fisch, et al. reference demonstrates that the distrontium salt of 2-[N,N-di(carboxymethyl)amino]-3-cyano-4-carboxymethyl-thiophene-5-carboxylic acid exhibits excellent gastroesophageal tolerance, whereas strontium chloride exhibits ulcerogenic activity. These superior and unexpected effects are not taught or suggested by the cited references, alone or in combination.

Thus, the Applicants respectfully submit that the instant claims are not rendered obvious by the disclosure of the cited references. Reconsideration and withdrawal of the obviousness rejection under 35 USC § 103(a) is respectfully requested.

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Accordingly, entry of present amendment, reconsideration of all grounds of objection and rejection, withdrawal thereof, and passage of this application to issue are all hereby respectfully solicited.

It should be apparent that the undersigned agent has made an earnest effort to place this application into condition for immediate allowance. If she can be of assistance to the Examiner in the elimination of any possibly-outstanding insignificant impediment to an immediate allowance, the Examiner is respectfully invited to call her at her below-listed number for such purpose.

Allowance is solicited.

Respectfully submitted,

THE FIRM OF HUESCHEN AND SAGE

By:

  
MICHELE M. CUDAHY, Reg. No. 55,093

Dated: August 8, 2008  
Customer No.: 25,666  
Seventh Floor, Kalamazoo Building  
107 West Michigan Avenue  
Kalamazoo, MI 49007  
(269) 382-0030

Enclosure: Form PTO-1449 and Accompanying Reference; Listing of Claims; and  
Postal Card Receipt

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